

Supporting Information

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SI Text

Task Training. Just before the fMRI task, extensive training (to decrease performance differences between the groups) was conducted outside and inside the scanner; the former was performed in front of a computer monitor in the MRI console area, whereas the latter was performed while subjects were supine in the MRI scanner replicating the exact task conditions but without MRI data collection. The training sequences were identical to the task sequences (Fig. S3B) except that, to decrease subsequent habituation effects, the letter “A” (and not words) was used. Subjects were also aware of not being paid for these training sequences that were repeated up to 3 times depending on performance (70% accuracy threshold). The number of training repetitions did not differ between the groups (outside scanner: 1.3 ± 0.09 ; inside: 1.3 ± 0.1 ; both $Z > 0.3$, $P > 0.5$).

Potential Impact on Results of Race and Cigarette Smoking. To control for the potential covariates, t-tests were conducted to inspect differences in the regions of interest (ROIs) as a function

of race and cigarette smoking (that differed between the study groups, Table S1). If significant across all study subjects ($P < 0.05$), these two variables were entered as separate covariates in the relevant ANOVA (1).

Results. Behavior. There were no differences in the behavioral variables (accuracy, reaction time, rating scales) as a function of history of cigarette smoking or race (t or $Z < |1.7|$, $P > 0.1$).

ROI analyses. Except for the cerebellum, activations in all ROIs did not differ by history of cigarette smoking ($t < |2.0|$, $P > 0.05$). The cerebellar group main effect remained significant after controlling for cigarette smoking ($F_{1,32} = 5.9$, $P < 0.05$). Race distribution differences were noted in the caudal-dorsal anterior cingulate cortex (cdACC), dorsolateral, and dorsomedial prefrontal regions. Including race as covariate, the group main effect remained significant in the cdACC and the dorsolateral prefrontal cortex ($F_{1,32} > 5.8$, $P < 0.05$).

Correlations. All correlations remained significant after controlling, with partial correlations, for history of cigarette smoking or race ($r > |0.66|$, $P < 0.01$).

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3. Wilkinson G (1993) *Wide Range Achievement Test, Administration Manual* (Wide Range, Wilmington, DE), 3rd Ed.
4. Wechsler D (1999) *Wechsler Abbreviated Scale of Intelligence* (Psychological Corporation, San Antonio, TX).
5. Beck AT, Steer RA, Brown GK (1996) *Beck Depression Inventory Manual* (Psychological Corporation, San Antonio, TX), 2nd Ed.
6. Kampman KM, et al. (1998) Reliability and validity of the Cocaine Selective Severity Assessment. *Addict Behav* 23:449–461.
7. Tiffany ST, Singleton E, Haertzen CA, Henningfield JE (1993) The development of a cocaine craving questionnaire. *Drug Alcohol Depend* 34:19–28.

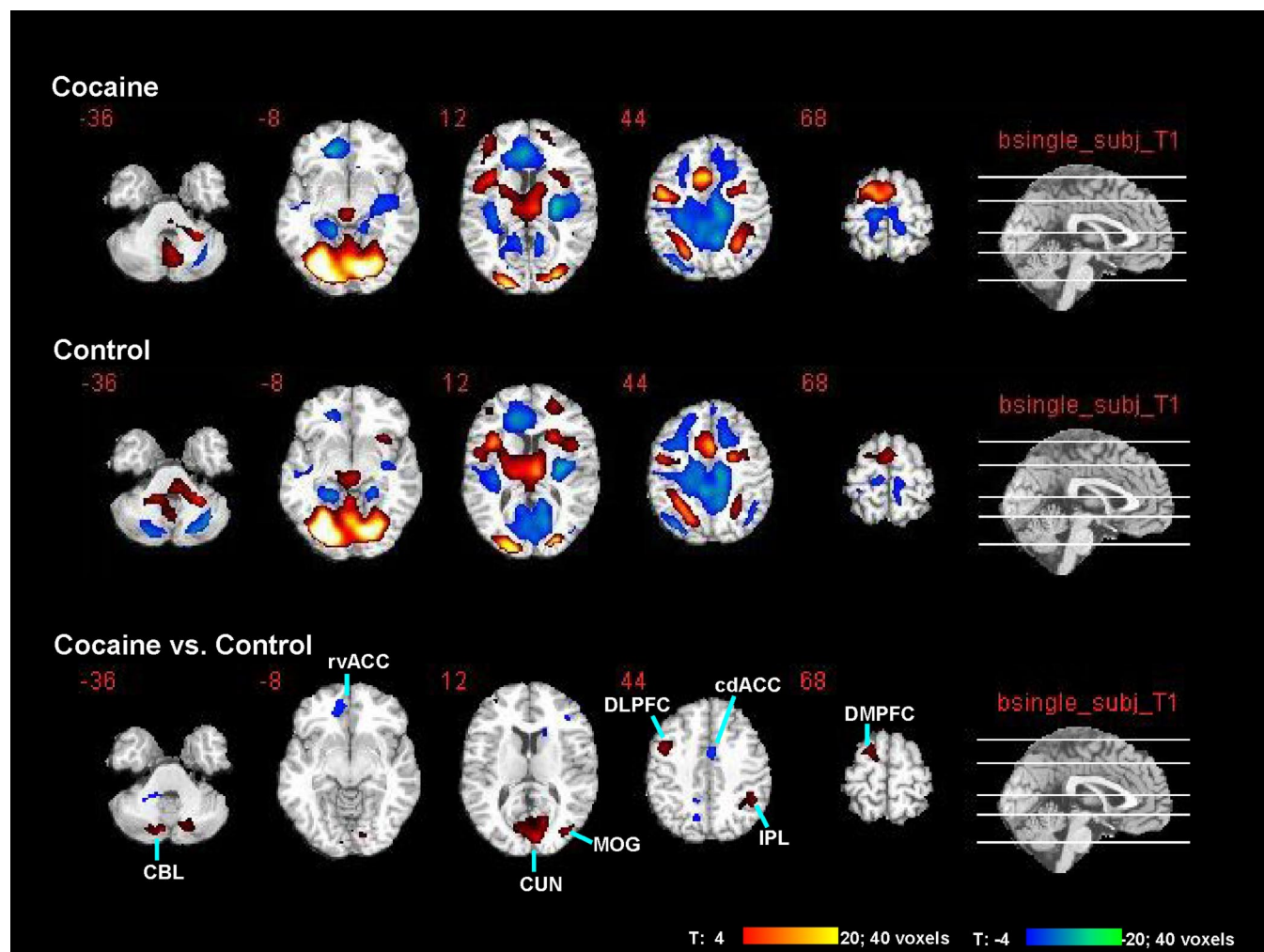


Fig. S1. Statistical maps of the average BOLD signal across all 4 task conditions (drug and neutral words at 0¢ and 50¢ reward condition) for 17 cocaine abusers (Top), 17 control subjects (Middle), and for the differential activation between the groups (Bottom). Red labels (Top) indicate the z-coordinate of each axial slice in millimeters in the Talairach frame of reference. White labels (see Fig. S2) and blue arrows indicate the BAs. Random effects analyses (repeated measures ANOVA). Red-yellow and blue-green color bars show the t-score windows for activation and deactivation, respectively.

Hyperactivations in Cocaine Addiction

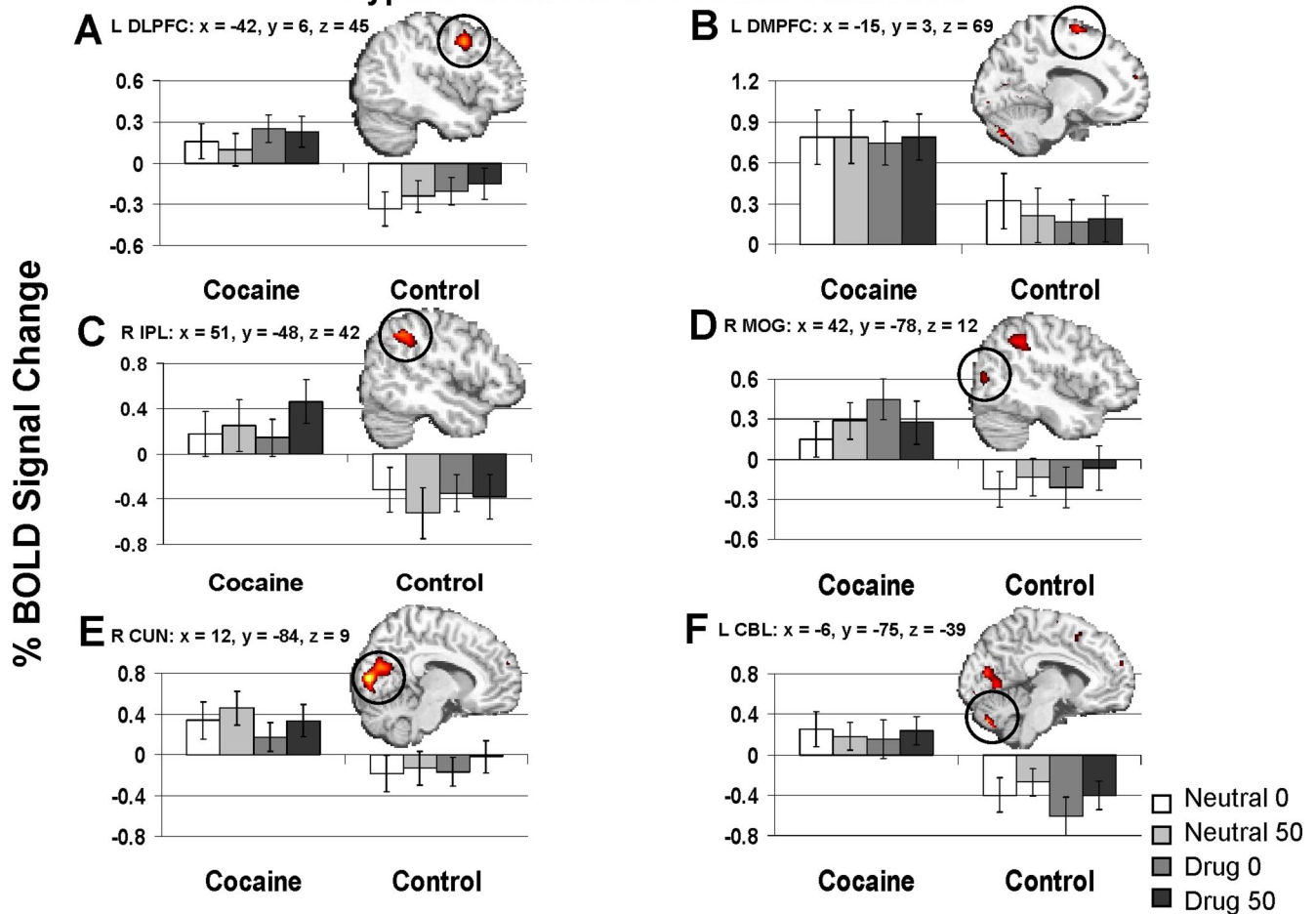
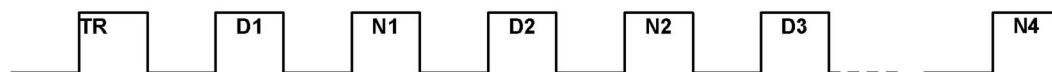


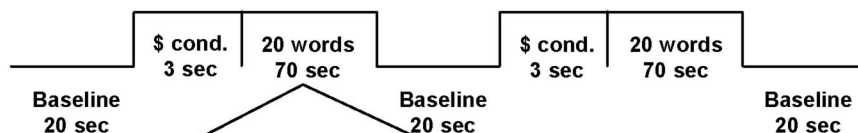
Fig. S2. Other cortical and subcortical hyperactivations in cocaine addicted as compared with control subjects ($n = 17$ in each group): mean % BOLD signal change from a fixation baseline as a function of the selected 4 task conditions in the left dorsolateral prefrontal cortex (L DLPFC, $x = -42, y = 6, z = 45$) (A); left dorsomedial prefrontal cortex (L DMPFC, $x = -15, y = 3, z = 69$) (B); right inferior parietal lobule (R IPL, $x = 51, y = -48, z = 42$) (C); right middle occipital gyrus (R MOG, $x = 42, y = -78, z = 12$) (D); right cuneus (R CUN, $x = 12, y = -84, z = 9$) (E); and left cerebellum (L CBL, $x = -6, y = -75, z = -39$) (F). Error bars represent standard error of the mean. The respective sagittal maps show the maxima of the selected ROIs ($P < 0.001$ familywise cluster-level corrected, 20 voxels minimum) that represent the regions that significantly differed between the groups in the second-order group ANOVA as described in *Methods*. Note that in all ROIs, except for the left dorsomedial prefrontal cortex (B), the group main effect survived corrections for covariates (see previous discussion).

fMRI Task

A. All 8 sequences (total 27.2 min):



B. Each drug or neutral 3.4-min sequence (2 blocks):



C. Each 3.5-sec trial:

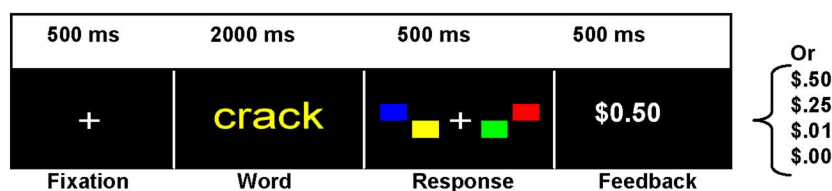


Fig. S3. fMRI task design. (A) There were eight 3.4-min-long sequences. (B) Each sequence contained 2 blocks with 20 matched drug or neutral words, interleaved with a 20 s fixation cross. Every block was preceded by a 3,000 ms window informing subjects of the amount of monetary reward to be gained for correct performance on every trial in that block. (C) Each trial comprised a 500 ms fixation cross, a 2,000 ms word presentation, a 500 ms response window, and a 500 ms monetary feedback. Subjects had to press 1 of 4 response buttons (yellow, blue, red, green) during the response window, matching the color of the word they had just read. There were 4 different monetary feedback conditions (50¢, 25¢, 1¢, 0¢). In case of an error (omission or commission), subjects saw an X. Subjects received up to \$75 for this task, an amount that was entirely contingent on performance (i.e., a single error in the 50¢ condition resulted in deduction of this amount from the total possible gain). For simplicity and clarity, here we report results of 4 sequences: 2 of the monetary conditions (the highest reward and a neutral cue: 50¢ and 0¢) performed twice (drug vs. neutral words).

Table S1. Demographics, drug use, and task-related measures of all study subjects

	Test	Cocaine (N = 17)	Control (N = 17)
Demographics			
Gender: male/female	$\chi^2_1 = 0.2$	13/4	14/3
Race: African-American/other (Caucasian/Hispanic)	$\chi^2_1 = 5.9^*$	16/1 (0/1)	10/7 (6/1)
Laterality Quotient (2)	$Z = -0.4$	0.91 ± 0.02	0.92 ± 0.03
Age, years	$t_{32} = 1.8$	43.3 ± 1.5	39.0 ± 2.0
Education, years	$Z = -2.0$	13.2 ± 0.4	14.4 ± 0.5
Verbal IQ: Wide Range Achievement Test III - Reading Scale (3)	$t_{32} = -1.0$	99.5 ± 2.4	102.9 ± 2.3
Nonverbal IQ: Wechsler Abbreviated Scale of Intelligence - Matrix Reasoning Scale (4)	$t_{32} < 0.01$	10.9 ± 0.5	10.9 ± 0.7
Depression: Beck Depression Inventory II (5)	$Z = -0.7$	4.9 ± 1.3	3.1 ± 0.8
Socioeconomic Status: Hollingshead Index	$t_{32} = -1.3$	32.5 ± 3.0	38.5 ± 3.5
Drug Use			
Cigarette smokers (current or past/nonsmokers)	$\chi^2_1 = 7.6^{**}$	13/4	5/12
Daily cigarettes (current smokers: N = 12/4)	$t_{32} = 0.4$	9.7 ± 1.7	8.3 ± 2.3
Time since last cigarette (within 4 h / >4 h/overnight or more)	$\chi^2_2 = 2.3$	6/4/2	1/3/0
Age of onset of cocaine use (years)	—	23.9 ± 1.6	—
Duration of cocaine use (years)	—	16.5 ± 1.4	—
Days/wk of cocaine use during the last 30 days	—	3.4 ± 0.5	—
Duration of current abstinence/time since last use (days)	—	4.6 ± 1.0	—
Withdrawal symptoms: 18-item CSSA (0–126) (6)	—	12.5 ± 2.1	—
Cocaine craving: 5-item Questionnaire (0–45) (7)	—	16.8 ± 2.2	—
Task-related measures			
Behavior: accuracy, drug words 0¢	$Z = -0.5$	17.1 ± 0.5	16.7 ± 0.5
Behavior: accuracy, drug words 50¢	$Z = -0.6$	17.3 ± 0.6	18.2 ± 0.3
Behavior: accuracy, neutral words 0¢	$Z = -0.7$	17.2 ± 0.6	16.8 ± 0.5
Behavior: accuracy, neutral words 50¢	$Z = -0.5$	17.9 ± 0.4	17.8 ± 0.4
Behavior: reaction time, drug words 0¢	$t_{32} = -1.4$	248.9 ± 6.7	260.5 ± 4.8
Behavior: reaction time, drug words 50¢	$t_{32} = -0.3$	246.7 ± 7.7	250.0 ± 7.6
Behavior: reaction time, neutral words 0¢	$t_{32} = -0.3$	252.9 ± 9.3	256.0 ± 6.2
Behavior: reaction time, neutral words 50¢	$t_{32} = -0.1$	253.5 ± 5.6	254.6 ± 6.2
Amount earned on the task, dollars	$t_{32} = -0.6$	67.1 ± 1.4	68.1 ± 0.9
Ratings: want money (0–10) [†]	$Z = -0.4$	7.9 ± 0.5	8.1 ± 0.6
Ratings: want cocaine (0–10)	$Z = -3.5^{**}$	2.2 ± 0.6	0.7 ± 0.07
Ratings: change in wanting cocaine (after minus before fMRI task: decrease or no change/increase)	$\chi^2_1 = 6.9^{**}$	11/6	16/0
Ratings: change in wanting money (after minus before fMRI task: decrease or no change/increase)	$\chi^2_1 < 0.1$	14/3	13/3
Ratings: value of drug words (–5–+5)	$Z = -0.1$	-1.5 ± 0.3	-1.7 ± 0.3
Ratings: value of neutral words (–5–+5)	$Z = -0.7$	0.5 ± 0.3	0.7 ± 0.3

CSSA, Cocaine Selective Severity Assessment Scale. χ^2 tests were used for categorical variables; t tests or nonparametric Mann–Whitney U were used for continuous variables. Means \pm SEM. *, $P < 0.05$; **, $P < 0.01$.

[†]Data for one control subject is missing for these ratings.